REMARKS

A. A Method For Treating Sleep Apnea Is Patentably Distinct From A Method For Treating Snoring

Applicants note the Examiner's remarks "that snoring is a symptom of an obstructive sleep apnea". However, Applicants request reconsideration that a treatment for snoring anticipates a treatment for sleep apnea.

a. Snoring And Sleep Apnea Are Recognized As Distinct Conditions

One estimate states that only 10% of snorers have sleep apnea. See, Huang, et al., "Biomechanics of Snoring", Endeavor, pp. 96 – 100, Vol. 19, No. 3 (1995), first page, column 1 (cited in present application and copy enclosed for the Examiner's convenience). Snoring is a poor predictor of sleep apnea since snoring is so common in the general population. Schlosshan et al., Clinical Presentation and Diagnosis of the Obstructive Sleep Apnoea Hypopnoea Syndrome", Thorax, pp. 347 – 351 (2004) (copy enclosed). While recognizing that most (but not all) sleep apnea patients snore, Schlosshan et al. describe clinical diagnosis based on a combination of habitual load snoring and frequent breathing pauses with a full sleep study (i.e., polysomnography) regarded as the "gold standard for the diagnosis ... ." (p. 349, col. 1)

As a result of the complexity of sleep apnea and the unreliability of snoring alone, it would not be obvious to one of ordinary skill in the art to turn to a snoring treatment to treat obstructive sleep apnea.

b. The FDA Recognizes That An Effective Snoring Treatment Does Not Suggest Effectiveness As A Sleep Apnea Treatment

The assignee of the present application and the Conrad et al. patent has sought clearance (under so-called 510(k) clearance) through the U.S. Food and Drug Administration to market a palatal implant for both snoring and sleep apnea.

After applying for a clearance with data indicating abatement of snoring, the FDA issued 510(k) No. K011723 for treating snoring on December 18, 2002. A copy of the indication for use for K011723 is enclosed.

Only after submission of additional data with a new 510(k) application did the FDA issue 510(k) No.040417 for treating obstructive sleep apnea. A copy of the indication for use for K040417 is enclosed.

The FDA's requirement of two separate applications (with supporting data) for treatment of snoring and sleep apnea is evidence that a method for treating snoring is not the same as or suggestive of a method for treating obstructive sleep apnea.

c. Scientific Literature Supports A Recognition In The Art That A Snoring Treatment Does Not Suggest Its Use In A Sleep Apnea Treatment

Enclosed is a copy of Blumen, et al., "Radiofrequency Ablation for the Treatment of Mild to Moderate Obstructive Sleep Apnea", Laryngoscope, pp. 2086 – 2092 (2002). That article (published after Applicants' effective filing date) notes that a radiofrequency (RF) ablation of the soft palate had been used to treat snoring but without a significant reduction in obstructive events (p. 2086, col. 2, 2nd para.). The article also notes that historically, UPPP (surgical removal of a portion of a trailing end of the soft palate) was the only soft palate surgical technique recommended by the American Sleep Disorders Association (p. 2089, col. 2, 2nd para.). Additionally, the article notes that reduction of snoring is not, by itself, a cure for sleep apnea (p. 2091, col. 1, 3rd para.). The article does note that RF ablation of the soft palate in some patients is a effective treatment for OSA (Conclusion, p. 2091, col. 2).

The Blumen et al. article further establishes that a snoring treatment does not show or suggest a sleep apnea treatment since:

1. With the exception of highly invasive UPPP, soft palate treatments were not recommended in the art for treating sleep apnea;
2. Reduction in snoring is not by itself evidence of successful treatment of sleep apnea; and
3. An RF soft palate snoring treatment which also treated sleep apnea was a surprising result.

d. Amendments To Claim 1

Claim 1 is amended to correct the informality noted by the Examiner

Claim 1 is also amended to incorporate into the body of the claim as well as the preamble that the method of treatment is to treat obstructive sleep apnea on sleep apnea identified patients.

B. Terminal Disclaimer

Enclosed is a terminal disclaimer with reference to U.S. Pat. Nos. 6,431,174; 6,250,307 and U.S. Pat. No. 6,513,530 to overcome double patenting rejections raised by the Examiner.

For the reasons given above, Applicants respectfully submit this application is in condition for allowance. Reconsideration and Notice of Allowance are solicited.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

Date: 2 September 2004

Timothy R. Conrad
Reg. No. 30,164
TRC:PLSkaw

Biomechanics of snoring

Lixi Huang, S. James Quinn, Peter D.M. Ellis and John E. Ffowcs Williams

A large proportion of the population either snores or suffers the snoring of others. Recent advances with the use of fibre-optic endoscopes have enabled surgeons to observe the inside of the pharynx while a patient is asleep and snoring. In this article we look at the underlying structure of the upper airway and explain, with the use of simple mechanical models, the aerodynamic events occurring inside the upper airway during snoring.

Up to 20 per cent of the adult population snore habitually [1] and it is not uncommon in children. It is likely that man has found the snoring of others unpleasant since cave-dwelling times, but it was not until the second half of this century that effective medical and surgical treatments were developed. The sound of snoring consists of a series of impulses caused by the rapid obstruction and reopening of the upper airway. This cycle of closure and opening occurs in the region of fifty times per second during a snore. In most cases, loud snoring does not pose any health threat although it is a frequent cause of marital disharmony. In 10 per cent of habitual snorers, complete collapse of the airway during sleep leads to the obstructive sleep apnoea syndrome. Due to adverse effects on the cardiovascular system and daytime tiredness, this disease has been linked with higher than average rates of death from both accidental and natural causes [2]. In the last ten or so years there has been an increasing awareness in the general population of the problems of loud snoring and obstructive sleep apnoea, and doctors have been seeing a much greater demand for medical and surgical treatment. In this article we have combined our experiences from the clinical observation of snoring in adults with an explanation of the suggested underlying mechanics.

Lixi Huang, Ph.D.

Is a graduate of Beijing University of Aeronautics & Astronautics. His Ph.D. was awarded by Cambridge University on the subject of acoustics. He has been a College Research Fellow on biofluid mechanics at Peterhouse, Cambridge, since 1992.

S. James Quinn, FRCS

Is a graduate of Guy's Hospital, London University. He trained in otolaryngology in London and Cambridge and has been a lecturer in otolaryngology at the Royal London Hospital, Whitechapel, since 1993.

Peter D.M. Ellis, FRCS

Is a graduate of Cambridge University. He has been a consultant surgeon in otolaryngology at Addenbrooke's Hospital, Cambridge, since 1977.

John E. Ffowcs Williams, Ph.D., D.Sc., F.Eng.

Has been the Rank Professor of Engineering (Acoustics) at the University of Cambridge since 1972.

Clinical studies

The structure of the upper airway in humans is fairly uniform (Figure 1). Air may enter either through the mouth or the nose or through both simultaneously. The nose can be thought of as a rigid tube through which air flows. It is a site of significant airflow resistance but it has bony walls and is not prone to collapse. After passing through the mouth or nose, air enters the pharynx. The soft palate lies at the upper end of the pharyngeal airway and acts as a flap or valve which closes off the nasal airway during swallowing to prevent the regurgitation of food into the nose. It also regulates the amount of air escaping via the nose during speech. The pharynx accommodates both the passage of air while breathing and the passage of food while swallowing. To perform both these functions it takes the form of a soft, distensible, and collapsible tube which is held open by the action of the pharyngeal muscles. At the lower end of the pharyngeal airway lies the larynx. Here the air and food passages split. Food passes down into the oesophagus on the way to the stomach. Air passes through the larynx into the trachea, and on down to the lungs. The larynx and trachea contain a strong framework of cartilage and are not prone to collapse under normal circumstances. The upper airway can therefore be thought of as a tube with two openings at the upper end and one at the lower end. This tube is rigid at both ends but flexible in its mid section (Figure 2). A flexible flap (the soft palate) sits at the junction where the two openings of the upper end of the airway join to form a single channel. It is the

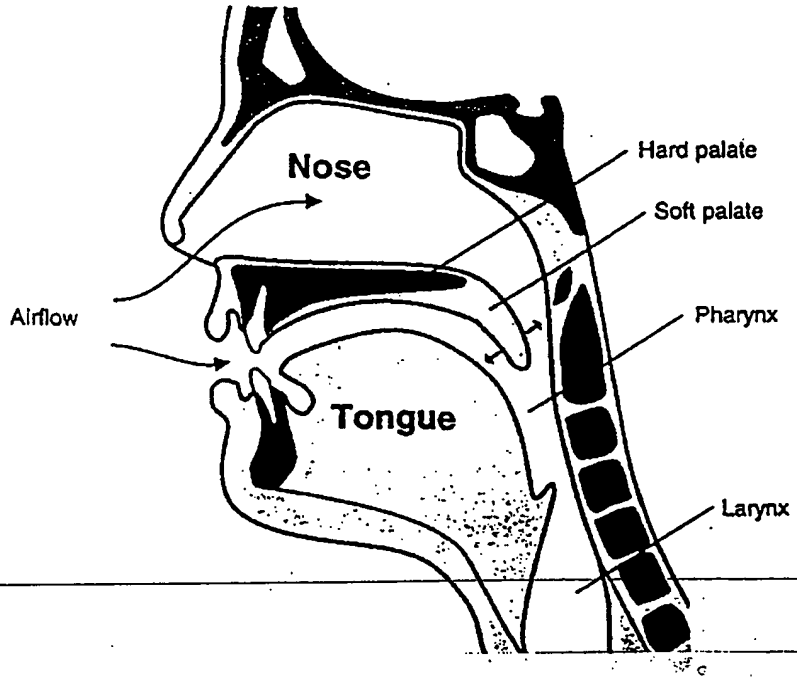


Figure 1 The anatomy of the human upper airway

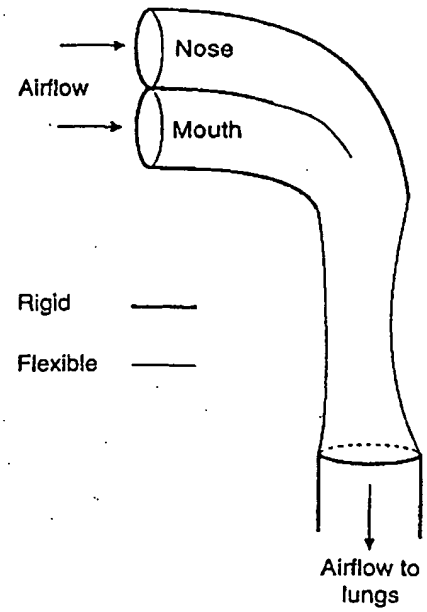


Figure 2 Schematic representation of the upper airway.

compromise in structure required to accommodate the efficient passage of solid and liquid food which result in the tendency of the pharyngeal airway to collapse during inspiration with the resulting phenomena of snoring and obstructive sleep apnoea.

Examination of the dynamic events occurring inside the airway while a subject is asleep and snoring is difficult. Recently a technique called sleep nasendoscopy has been described [3]. This technique allows the direct visualization of the interior of the pharyngeal airway while the subject remains asleep. The subject is sedated with a hypnotic drug, and a thin and flexible fibreoptic endoscope is passed via the nasal cavity into the pharynx. We have observed several different types of snoring using sleep nasendoscopy. The majority of snoring in the human adult is caused by the soft palate flapping backwards and forwards in the airway. Two types of soft palate vibration have been observed. In one, the mouth is closed and air is drawn into the lungs through the nose. In this case, a cycle of vibration consists of the trailing edge of the soft palate being sucked into the nasopharyngeal space and briefly obstructing the airway before dropping back down on to the tongue below. The second type of vibration occurs when the mouth is open and air is drawn both over the upper surface of the soft palate via the nose and over the lower surface via the mouth. The soft palate in this case flaps up and down between the tongue and posterior pharyngeal wall, briefly obstructing the oral and nasal airways in turn. In a smaller proportion of people, snoring may be caused by collapse of the pharyngeal airway below the level of the soft palate but above the level of the larynx. The component most subject to collapse is circular or tube-like but, because of variations in the wall of the pharynx caused by the presence of the tonsils and tongue-base, the direction of collapse varies between individuals and may be either from side to side or front to back.

The medical treatment of airway collapse has centred around the use of a technique known as nasal continuous positive airway pressure (CPAP). Nasal CPAP is very effective [4]. It works by splinting open the collapsible pharynx by maintaining an increased air pressure inside the pharynx during breathing. The user wears an airtight mask over the nose. The mask is attached to a pump which pumps air into the mask at a constant pressure (Figure 3). The mask contains two valves which ensure that inspired air comes from the pump and that expired air is vented to the atmosphere. One valve (valve b in Figure 3) opens only when the pressure inside the mask exceeds around 5 cm of water pressure above atmospheric pressure. This ensures that the pressure inside the nose and upper airway does not fall below atmospheric pressure during the breathing cycle, and so collapse of the pharynx is prevented during inspiration. The mask is strapped to the subject's head and is worn all night long. Nasal CPAP effectively stops both snoring and obstructive sleep apnoea. However, the equipment is bulky, expensive, and somewhat noisy, and its use is therefore restricted to patients with obstructive sleep apnoea severe enough to threaten their general health.

The traditional surgical procedure for reducing heavy snoring is called the uvulopalatopharyngoplasty [5]. This operation involves removing 2 cm of the trailing edge of the soft palate (cf. Figures 1 and 6(a)) thereby reducing its ability to flutter between the tongue and pharyngeal wall. This operation is effective but painful and may also have considerable unwanted side-effects [6].

It is hoped that study of the biomechanics of snoring will help to produce further advances in treatment in the future. In this article we now explore the underlying mechanics for two types of observed snoring phenomena using mechanical models. The first type of snoring that we explore is that involving flutter of the soft palate; the second is that caused by collapse and vibration of the pharyngeal airway.

Basic concepts

Snoring, and indeed respiratory noise in general, is caused by the coupled oscillation of the walls of the airway with the airflow through it. From the point of view of mechanics, these are problems related to the stability of flows over flexible structures. In the study of fluid–structure interactions, linear analyses play a vital role, although quantitative results call for the inclusion of non-linear effects. Linear analysis investigates the behaviour of very small disturbances to an otherwise steady state. Within this theoretical framework two distinct types of instability emerge. One is called 'static divergence' and the other is called 'dynamic instability' or 'flutter'. The basic concepts of the two types of instability are well demonstrated by the behaviour of the mass–spring system shown in Figure 4. As the suspended ball is displaced downwards by an applied force F, the spring tends to hold it back and acts to return the ball to its equilibrium position E. If the applied force F grows linearly as the ball is displaced further away from E, then the applied force can be viewed as though it originated in a spring of negative stiffness. In other words, the applied force can be viewed as if

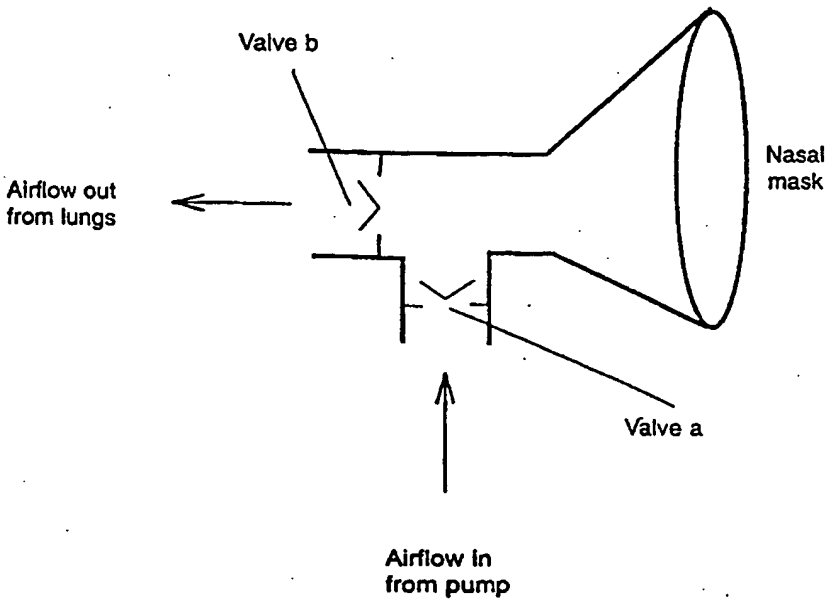


Figure 3 Diagram demonstrating the flow through a nasal CPAP mask. Air is inhaled from the pump via valve a. Exhaled air from the lungs is vented to the atmosphere via valve b.

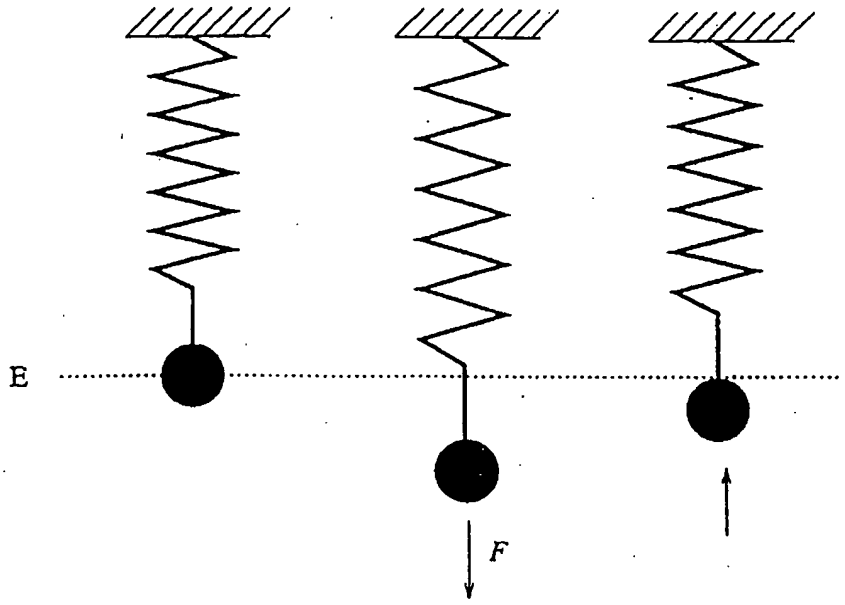


Figure 4 The stability of a ball attached to a spring. E is the equilibrium position; F is an applied force which displaces the ball from its equilibrium position.

it originated in a second spring whose direction of action is always opposite to the original spring. If this second or negative spring is stronger than the existing positive spring

en, once the ball is displaced from its equilibrium position E, the net force pulls the ball further away from E. The ball does not return to E but instead accelerates away until the spring, and indeed the linear theory, breaks down. The positional instability that occurs in this way is described as static divergence.

If, on the other hand, the system is such that the total stiffness remains positive, then when the ball is released from a displaced position it will come back to E. However, due to its inertia, it will overshoot across the equilibrium point. In the absence of any damping, the ball would overshoot by the same displacement in the other direction, and a cycle of oscillation would become established which would go on for ever. In the presence of damping, kinetic energy is lost and the oscillation cycle decreases until the ball finally comes to rest at E. If, however, the damping were negative, then, rather than decreasing with each cycle, the amplitude of oscillation would grow instead. This phenomenon is known as 'flutter'. Since it is not easy to imagine that damping can be negative, consider an example of flutter induced by a spring with a special property. This spring acts in the same direction as the original spring but has a small time delay before it acts to restore the ball to its equilibrium position. When the ball reaches its equilibrium position E, because of the time delay the spring still has a force pulling the ball further across the equilibrium point as if the ball had not yet reached it. The delayed action of the spring transfers energy into the system and the amplitude of the oscillation will grow cycle by cycle.

Both flutter and static divergence occur in snoring. The following mechanical models demonstrate how they occur in the soft palate and in the walls of the pharynx.

Model of palatal snoring

In this model we simulate the movement of the soft palate in palatal snoring (Figure 5). The model represents human breathing in through both mouth and nose with the inspired air flowing over the upper and the lower surfaces of the palate. The hard palate is rigid and bony and is simulated in our model by a thin plate of wood. The soft palate is soft and flexible and is represented by a piece of soft leather. The wooden 'hard palate' and leather 'soft palate' are attached to each other and are set inside a rigid Perspex tube. The tube is connected to a suction pump to simulate the action of the lungs during inspiration. Below a critical flow speed, the soft palate remains still. Once the speed is exceeded, the soft palate flaps violently back and forth, hitting the sides of the tube. Careful observation, confirmed by photographic evidence, reveals that the flap of the soft palate actually starts as small-amplitude oscillations which increase in size over several cycles until the tube wall is hit. This conforms with the concept of flutter [7]. In order to understand this mechanism we first compare the soft palate to a flat wing section, the stability of which is well understood. A lifting force is exerted by the airflow over the wing if the wing swings across the direction of flow. This force acts to restore the wing to its central equilibrium position. An essential condition for this restoration is that the wing remains straight. If, in our model, we replace the flexible leather used for the soft palate with a rigid plate hinged to the hard palate, then we find that the plate does stay still regardless of the speed of flow over it. The distribution of the lift force is such that it is highest at the leading edge and disappears towards the trailing edge. When the wing is flexible then its flatness will not be maintained under the action of these aerodynamic forces. The distribution of the lift force tends, therefore, to bend the soft palate.

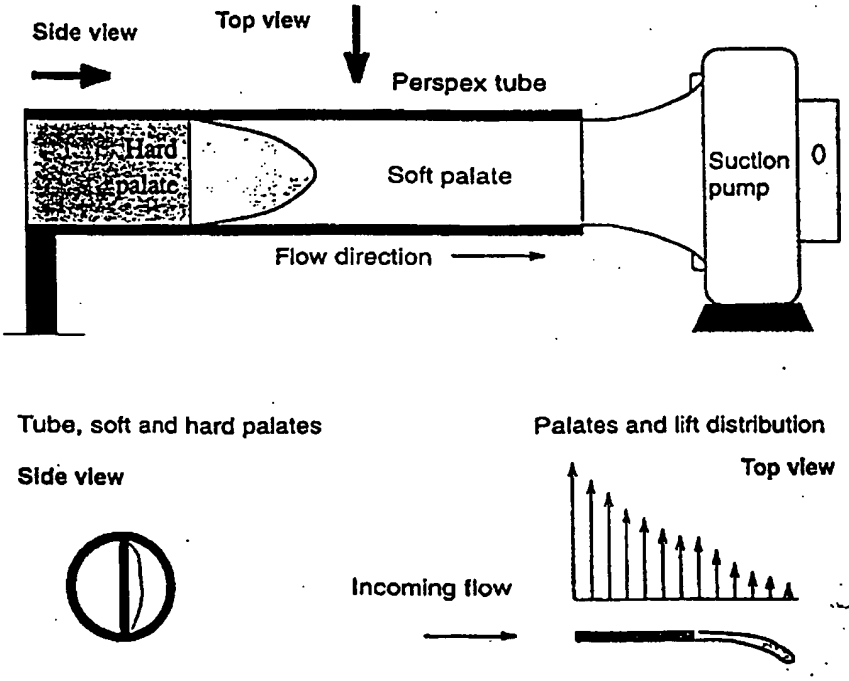


Figure 5 The experimental model to simulate palatal snoring, and a diagram demonstrating the lifting forces on the palate.

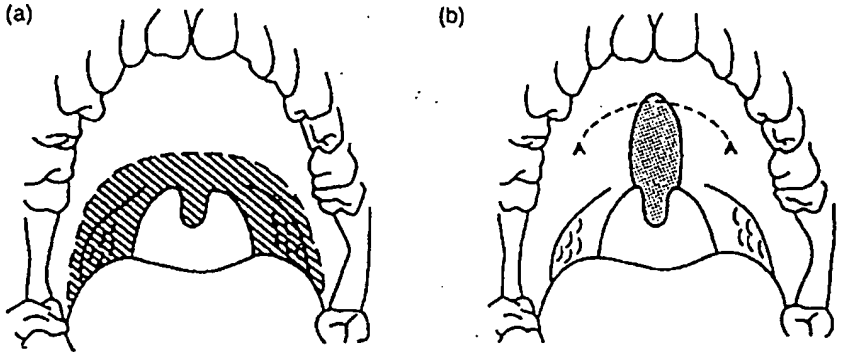


Figure 6 Diagrammatic representation of the roof of the mouth. The shaded area in (a) demonstrates the area of soft palate excised in the uvulopalatopharyngoplasty operation. The stippled area in (b) demonstrates the area of creation of scar tissue in the new operation. The dashed line in (b) denotes the junction of the hard and soft palates.

Let us now treat the soft palate as the ball in the previously described mass–spring system, with its natural stiffness acting as the spring which holds it in the equilibrium position. Any displacement of the palate leads to the generation of lift, and this displacement-induced force contributes to the effective stiffness of the system. Aerodynamic considerations tell us that the force is basically dependent upon the angle at which the surface attacks the incoming flow. Due to the non-uniform force distribution, the upstream part of the soft palate responds first and the trailing edge lags behind. This means that the lift force, when viewed as an aerodynamic spring, has a delayed response to the motion of the soft palate as a whole. The result is a net transfer of kinetic energy from the airflow to the oscillating soft palate. The amplitude of oscillation increases from cycle to cycle, consistent with our earlier explanation of flutter. The oscillation amplitude is limited by the walls of the surrounding tube, and once the oscillation has reached its full amplitude impulsive noise is created as the soft palate hits the wall of the tube. The impulsive waveform of this model is shared both with the acoustic waveform of our rubber tube model for pharyngeal snoring (which is described in the next section) and also with the acoustic waveform of the human snoring sound. The palatal impulses are caused by the sudden cessation of local airflow as the trailing edge of the palate makes contact with the wall of the tube.

Once we have described the mechanics we can explore ways of reducing the tendency of the soft palate to flap. It is clear that both the length of the soft palate and its flexibility have fundamental effects on the critical flow speed at which flutter will occur. Shortening the soft palate, as is done with the uvulopalatopharyngoplasty operation (Figure 6(a)), effectively raises the critical flow speed and reduces or abolishes palatal flutter during inspiration. However, as we have mentioned previously, the soft palate performs an important function in closing off the nose from the mouth during swallowing and speech. Shortening of the soft palate in this way compromises the function of the soft palate, and in some 25 per cent of treated subjects this leads to the escape of fluids from the mouth into the back of the nose while drinking [6].

After studying the movement of the soft palate during snoring and examining the theoretical methods to reduce the tendency of the palate to flap, an operation was proposed to modify the function of the soft palate [8]. Reducing the flexibility of the soft palate as we have mentioned above should reduce palatal flutter. As the soft palate would not be shortened its function as a valve should not be impaired. With this in mind, a surgical laser was used to create scar tissue on the surface of the soft palate to stiffen it. This was achieved by removing a broad strip of mucosa, but not the underlying muscle, in a sagittal direction from the lower surface of the soft palate (Figure 6(b)). This produces an ulcer on the lower surface of the soft palate. As the ulcer heals over the next couple of weeks, so scar tissue is laid down which reduces the flexibility of the soft palate. A surgical laser is used because it produces a virtually bloodless field and reduces swelling and pain in the early postoperative period. Initial results from using this technique have been promising, with a complete or near-complete reduction in snoring in three-quarters of subjects and a much lower level of side-effects when compared with the uvulopalatopharyngoplasty operation. In particular, none of the patients who have had this operation under our care have experienced the nasal regurgitation of fluids.

Model of pharyngeal snoring

This model simulates the rhythmic collapse and opening of the pharynx observed during pharyngeal snoring. The pharyngeal airway is represented by a compliant tube which will collapse under a certain pressure differential. The tube, made of thin rubber, is of finite length with its upstream end open to the atmosphere and its downstream end connected to a suction pump as shown in Figure 7. The pump represents the suction effect of the lungs during inspiration. When the air flows, its pressure falls from p_o to p

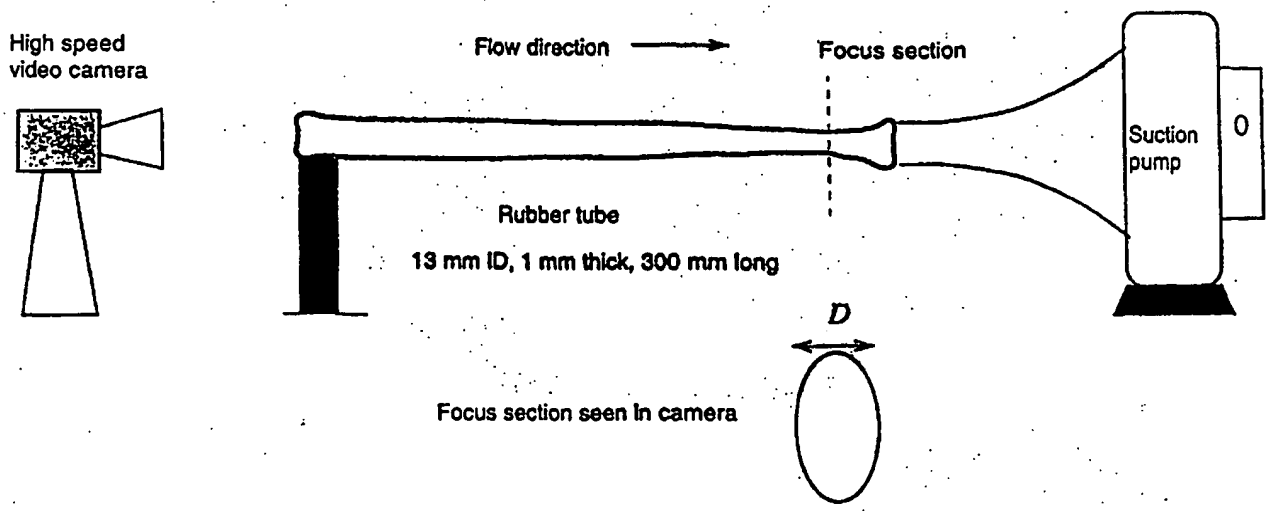
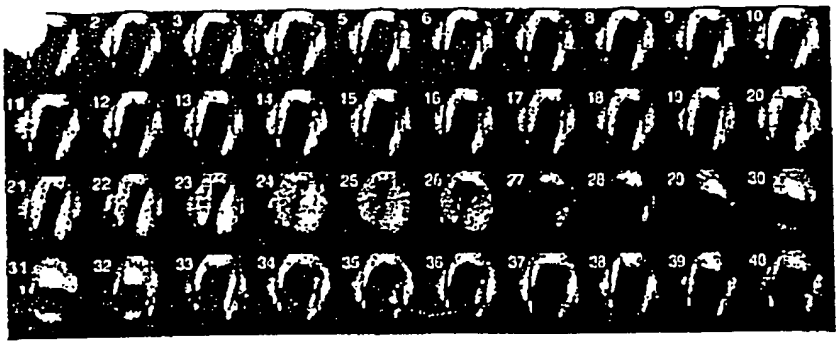


Figure 7 The experimental model to simulate inspiratory flow through the pharynx.



Photos of consecutive frames

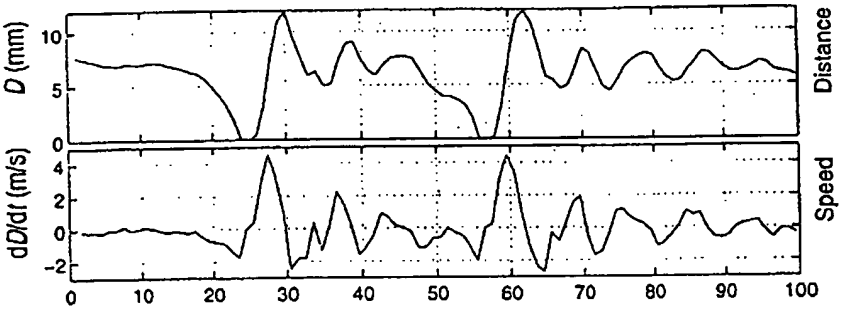


Figure 8 Consecutive frames of high-speed video filming of a collapsing tube conveying airflow, and graphs demonstrating the variation over time of the distance D between the two opposite sides and the speed of movement of the walls, dD/dt.

as part of its energy is converted into the kinetic energy of motion. The Bernoulli equation gives $p = p_o - \frac{1}{2}\rho u^2$, where ρ and u are the air density and flow speed respectively. The air pressure outside the tube is the constant p_o, and the pressure difference $p_o - p$ tends to collapse the tube. In addition to this inviscid pressure drop, there is a friction force between the wall of the tube and the airflow which causes the pressure to drop along the flow path. The pressure is lowest therefore at the downstream end. As the airflow speed is increased and the internal pressure falls, the limit of the tube's circumferential strength is first reached near its downstream end, although not at the very end as the tube is supported there by its attachment to the rigid entrance of the pump. At first the tube section becomes elliptical, with smaller cross-sectional area than the circle of the same periphery. This narrowing of the airway causes the flow to speed up, with the same mass flow passing through the narrowed section but at a faster speed. This, in turn, leads to a further reduction in the local pressure, and so on. The result is that the section will collapse completely in an accelerating manner until the opposing sides of the tube hit each other. This is a typical case of static divergence. But there are many ways of looking at this problem, and there are additional effects that prevent the two sides from going all the way towards collision. A flutter-type of instability can occur prior to total collapse [9,10]. That phenomenon where flutter precedes total collapse is known as 'post-divergence flutter'.

In search of evidence of post-divergence flutter, we performed an experiment where internal flow caused the collapse of a rubber tube constructed to model the pharynx. We observed the tube and recorded its shape using a high-speed video camera (EKTAPRO EM, Kodak, Rochester, New York) at a rate of 1000 frames per second. The lens was focused on the inner surface of the collapsing section of the tube. The consecutive frames before and after the two sides of the tube first come into contact are displayed in Figure 8. The distance between the two sides of the collapsing tube was measured, and its time history is consistent with the collapse continuing until contact is made. There was no evidence of flutter in our experiment.

What happens after complete collapse is striking. From the film and the measured data, we find that the tube reopens at more than twice its closing speed. We believe that this is caused by the very high positive internal pressure induced by the sudden interruption of the flow, a kind of 'water hammer' phenomenon. The sudden obstruction produces a shock that moves upstream to bring the flow to rest. The shock adjusts the flow speed to accommodate the blockage and produces very high internal pressures that force the tube to reopen rapidly. As the tube opens so it distends momentarily to greater than its original diameter due to the high local pressure. There then follows some four cycles of decaying local vibration in the tube wall which we believe to be the ringing of the suddenly expanded tube. Such a detailed examination of the movement of the pharynx in a human while snoring has yet to be performed, and may prove to be a big challenge.

Conclusion

In this article we have given a brief description of the events observed to occur in the human pharynx during snoring. Using simplified models of the pharynx we have explored the biomechanics of snoring for two distinct types of noise production. The instabilities in the structure of the pharynx which lead to snoring appear to be due to the phenomena of flutter and static divergence. We have also suggested that the 'water hammer' effect may have a role in the reopening of the momentarily occluded airway. By far the most common method of noise production in the human is that of palatal flutter. Our research has suggested to us a new method of treating palatal flutter snoring by stiffening rather than shortening the soft palate. Initial results for this procedure have been promising, but caution must always be observed with any new medical treatment as the long-term effects are not initially obvious.

Acknowledgements

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REVIEW SERIES

Sleep · 3: Clinical presentation and diagnosis of the obstructive sleep apnoea hypopnoea syndrome

D Schlosshan, M W Elliott

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Patients with OSAHS may present to a sleep clinic or to other specialists with symptoms that are not immediately attributable to the condition. The diagnostic methods available are reviewed.

The obstructive sleep apnoea hypopnoea syndrome (OSAHS) has been described as a public health problem comparable to smoking in its effects upon society.[1] However, it is largely unrecognised and undiagnosed.[2] Young *et al* estimated that 93% of women and 82% of men with moderate to severe OSAHS are not diagnosed.[3] Yet these patients are being seen by doctors on a regular basis; a telephone survey in the UK of approximately 5000 individuals aged 15–100 years found that 31% of those with breathing pauses during sleep had sought medical help more than six times in the previous 12 months compared with 12% of snorers and 11.9% of non-snorers. They sought medical treatment from their GP for a variety of physical complaints—not obviously related to a sleep problem—more than twice as often as patients without OSAHS.[2] The failure to recognise the syndrome is in part due to lack of training in sleep medicine (a study of all UK medical schools showed that students received a median of 5 minutes teaching in all aspects of sleep medicine throughout their training[4]) and a general lack of awareness. Many of the symptoms are non-specific and have other possible causes.[5] Failure to recognise OSAHS is costly both to the individual and to society; underdiagnosis is thought to cost the USA $3.4 billion in additional medical costs per year.[6] To this figure must be added the cost of losses in productivity, accidents, etc.[7 8]

Because OSAHS is so common, has considerable effects upon patients and their partners, increases the risk of other diseases, can be effectively treated, and is so often unrecognised, it is important to improve the way these patients are diagnosed. The first step is to increase awareness among doctors and the general public and for a simple sleep history to become part of the normal systems review taught at medical school.

This review will focus both on how patients present to sleep clinics and how they may present to other specialists with symptoms that are not immediately attributed to OSAHS.

See end of article for authors' affiliations

Correspondence to: Dr M W Elliott, Department of Respiratory Medicine, St James's University Hospital, Beckett Street, Leeds LS9 7TF, UK; mark.elliott@lineone.net

PRESENTATION TO SLEEP CLINICS

Patients are predominantly referred to a sleep clinic because they complain of excessive daytime sleepiness (EDS) or their partner complains about the noise of their snoring or expresses concern about witnessed apnoeas.[9]

Snoring

Snoring is very common in the general population; 35–45% of men and 15–28% of women report habitual snoring.[2 10] Loud intrusive snoring affects bed partners, family, and even neighbours. Noise pollution and its resulting social disability, relationship disharmony and threatened marriage break up[11] is an important reason why the patient, often pressurised by their partner, seeks medical help. In this case the "patient" is often more correctly the partner as the individual concerned is not aware of any adverse affects from his/her snoring other than the irritation reported by others. Snoring is also the most frequent symptom of OSAHS, occurring in 70–95% of patients,[12] but because it is so common in the general population it is a poor predictor of OSAHS.[13] However, the absence of snoring makes OSAHS unlikely; only 6% of patients with OSAHS do not report snoring,[14] but it should be appreciated that a patient's perception of his/her snoring may be inaccurate. Three quarters of patients who deny snoring turn out to snore when this is measured objectively.[15] Whenever possible, an account from a third party should be obtained.

Excessive daytime sleepiness

Excessive daytime sleepiness is caused by fragmented sleep related to frequent arousals. Like snoring, it is common and a poor discriminator of the patient with OSAHS. 30–50% of the general population without OSAHS report moderate to severe sleepiness.[10 16] It is important to differentiate true sleepiness (the urge to sleep) from various forms of tiredness such as lethargy, malaise or exhaustion. Patients themselves may underreport their sleepiness,[17] either because they are not aware of it or because there are social pressures to deny that it is a problem. They may not have considered other obvious causes of EDS such as drugs and shift work, and these

Abbreviations: AHI, apnoea/hypopnoea index; EDS, excessive daytime sleepiness; ESS, Epworth sleepiness scale; MSLT, multiple sleep latency test; MWT, maintenance of wakefulness test; ODI, oxygen desaturation index; OSAHS, obstructive sleep apnoea hypopnoea syndrome; PSG, polysomnography; RIP, respiratory inductance plethysmography; SDB, sleep disordered breathing

should always be asked about in the history. The possibility of dual causes such as shift work and OSAHS should also be considered.

Several tools are available for measuring sleepiness both subjectively and objectively. There is no gold standard, but the easiest and most practical is the Epworth sleepiness scale (ESS).[18] Drawbacks include poor correlation with the severity of OSAHS and the disadvantages that accompany any self-evaluated test such as misperception of sleep episodes and the possibility of cheating. The input of the partner is very useful.[19] The major advantages of the ESS are that it is simple, quick, inexpensive, and has a high test-retest reliability.[20] Objective tests have obvious advantages but are time consuming and may not reflect everyday activity. They include the multiple sleep latency test (MSLT),[21] the maintenance of wakefulness test (MWT),[22] and the Osler test.[23] Patients may also have neurocognitive deficits and psychological problems such as difficulty concentrating, poor memory, cognitive performance and personality changes with irritability and mood swings.[9] These problems may be of greater consequence to the patient than EDS, but routine psychometric assessment is not practical in clinical practice.

Witnessed apnoeas and nocturnal choking

Concern by the bed partner about breathing pauses witnessed during sleep is the third common reason for referral to a sleep clinic. However, bed partners rarely give a reliable account about apnoeas during sleep and even trained medical staff are poor at diagnosing respiratory events in patients with OSAHS through clinical observation.[24] Female patients with OSAHS are less likely to report nocturnal apnoeas[25 26] and witnessed apnoeas may be reported in up to 6% of the normal non-apnoeic population.[25] The patient may report waking up with acute panic and choking. These episodes usually only last for a few seconds but can cause considerable distress, both to the patient and the partner. They have to be differentiated from other causes of nocturnal breathlessness such as paroxysmal nocturnal dyspnoea in the patient with left ventricular failure, nocturnal asthma, acute laryngeal stridor, or Cheyne-Stokes respiration in patients with heart failure. Episodes of breathlessness in these conditions usually last longer and/or there is other evidence of the condition in question.

PRESENTATION TO OTHER SPECIALTIES

The pathophysiological consequences of OSAHS can affect almost every organ in the body and patients can present to other medical specialties with symptoms related to, caused by, or exacerbated by OSAHS.[27] It is important that clinicians are aware of the various ways in which OSAHS may manifest in their specialty, as in some cases treatment of the OSAHS results in an improvement in—or even complete resolution of—these symptoms.[28–30] Furthermore, treatment of some conditions such as hypothyroidism[31] and acromegaly[32] may result in resolution of OSAHS. It is beyond the scope of this review to describe in detail the presentation to various medical specialties but an overview is given in table 1.[33 34]

Table 1 How OSAHS might present to non-sleep specialists

	Presentation
Cardiologist[35–37]	Hypertension
	Left ventricular hypertrophy
	Nocturnal angina
	Myocardial infarction
	Arrhythmias, particularly bradyarrhythmias
	Heart failure
	Cor pulmonale
	Increased pulmonary artery pressure
Psychiatrist[38]	Depression
	Anxiety
	Behavioural problems
	Acute delirium
Neurologist[39–42]	Refractory epilepsy
	Stroke
	Impaired rehabilitation post stroke
	Headache on waking
Anaesthetist[43–45]	Difficult intubation
	Sensitivity to opioid analgesia and sedation
	Witnessed apnoeas during recovery
Urologist[46–48]	Nocturia
	Impotence
	Erectile dysfunction
Endocrinologist[31 32]	Hypothyroidism
	Acromegaly
	Diabetes
ENT surgeon[49]	Snoring
	Sore throat
	Hoarse voice
Gastroenterologist[50]	Oesophageal reflux
Haematologist[51]	Polycythaemia
Respiratory physician[52–57]	Nocturnal shortness of breath
	Respiratory failure

Box 1 American Sleep Disorders Association (ASDA) classification of OSAHS

- Sleepiness[58]
  - Mild: unwanted sleepiness or involuntary sleep episodes occur during activities that require little attention
  - Moderate: unwanted sleepiness or involuntary sleep episodes occur during activities that require some attention
  - Severe: unwanted sleepiness or involuntary sleep episodes occur during activities that require active attention
- Sleep related obstructive breathing events (apnoea, hypopnoea, and respiratory effort related arousals)
  - Mild: 5–15 events/hour of sleep
  - Moderate: 15–30 events/hour of sleep
  - Severe: > 30 events/hour of sleep[59]

DIAGNOSIS

The diagnosis of OSAHS is based on the characteristic clinical features together with objective demonstration of sleep disordered breathing (SDB). The American Sleep Disorders Association (ASDA) has proposed guidelines and a classification of severity of OSAHS (box 1).[20] This emphasises that the diagnosis of OSAHS is not based solely on the detection of respiratory events, but equally includes clinical factors such as sleepiness and impairment of social or occupational functioning.

Clinical assessment

Clinical assessment alone is not sufficient to make the diagnosis of OSAHS. Even sleep experts have been reported to be wrong in 50% of cases when making the diagnosis on history and examination alone.[14 15] None of the common presenting symptoms alone has sufficient discriminatory value to make an accurate diagnosis.[13] Combining constellations of symptoms can improve diagnostic accuracy. Loud

snoring and witnessed apnoeas identified OSAHS with a sensitivity of 78% and a specificity of 67%.[34] In a large study of 5000 subjects, those reporting habitual loud snoring and frequent breathing pauses were 3–4 times more likely to have an apnoea/hypopnoea index (AHI) of >15 than those who did not have any of these symptoms.[37] These findings are in keeping with results from previous studies.[13 14 36 38 39] Although obesity is an important risk factor for OSAHS, 50% of patients are not clinically obese (body mass index >30 kg^2).[40] Location of fat deposition, especially anterolateral to the upper airway, is more important.[40] Neck circumference has consistently been shown to be a strong predictor of OSAHS,[41 35] values of <37 cm and >48 cm being associated with a low and high risk, respectively. Certain craniofacial abnormalities are associated with OSAHS. Tonsillar hypertrophy, retrognathia, micrognathia, and certain facial configurations have been detected by cephalometry, MRI, or CT scans to be present in some patients with OSAHS,[42] but are of little predictive value. However, some are potentially amenable to surgical correction. Routine upper airway imaging is not currently recommended.

Clinical prediction models

Prediction models for both primary and secondary care that calculate the probability of a patient having OSAHS using self-reported symptoms combined with demographic and anthropometric data have been developed to try to improve the predictive value of clinical variables. With increasing recognition of OSAHS, the demand for diagnostic services is rising and such models may help to select patients for further evaluation. One author claimed that the number of polysomnographic investigations could be reduced by nearly 40% using one such model.[43] They are low cost and can be performed in the clinic; however, when tested prospectively, they have a high sensitivity (76–96%) but a low specificity (13–54%).[43] Furthermore, most have not been validated in populations such as the elderly, ethnic minorities, and in the primary care setting, in all of which the presentation of OSAHS may be very different from that seen in a sleep clinic.[44] Further validation of the clinical usefulness and cost effectiveness of such an approach is required.

Tests for sleep disordered breathing

Full polysomnography (PSG) is traditionally regarded as the gold standard for the diagnosis of OSAHS. Typically, it requires admission to hospital with a trained technician present throughout the night. It is time consuming, expensive, and the large variety of techniques, equipment, and diagnostic criteria used by different sleep centres make evaluation and comparison of PSG data difficult.[45] Redline *et al* showed that the respiratory disturbance index can vary 10-fold depending on the definitions of the respiratory variables used for the diagnosis of OSAHS. This could lead to a situation where the same patient could be diagnosed and treated in one centre and be declared not to have OSAHS in another.[46] Furthermore, PSG has not undergone the rigorous evaluation of accuracy, reliability, and validity expected for a "gold standard" diagnostic test.[45] The AHI, the primary index extracted from PSG, is poorly correlated with EDS, increases in normal people with age,[47] and has not been shown to predict short or long term morbidity or mortality. This leads some authors to question whether PSG can be regarded as a gold standard and reference tool when evaluating alternative diagnostic tests.[48 49]

There are two different aspects to full PSG—monitoring of various parameters reflecting respiration and monitoring cortical brain activity to assess the presence or absence of sleep and its stage. The constraints of space preclude a comprehensive review of all the various devices available for the investigation of SDB, but the most important issues will be addressed.

Monitoring of respiration

The diagnosis of SDB rests upon detecting changes in oronasal airflow and respiratory effort to define apnoeas and hypopnoeas. However, increased work of breathing usually, but not always, associated with loud snoring alone can lead to sleep disruption and daytime symptoms. This has been described as the upper airway resistance syndrome.[50] Whether it is part of the OSAHS spectrum or presents a distinct syndrome is controversial.[51 52] Classically, it requires measurement of changes in oesophageal pressure.[20 50] The definition of apnoeas and hypopnoeas is arbitrary and other respiratory effort related events[20] and episodes of inspiratory flow limitation may be important.

In patients with moderate to severe OSAHS the reproducibility of the respiratory parameters from night to night is good.[53] For milder OSAHS a single negative study may not exclude OSAHS and a second study should be considered.[54 55] Sleep position, acclimatisation to a foreign sleep environment, concurrent respiratory tract infections, and variable alcohol and drug use are thought to be responsible for night to night variability in both respiratory and sleep parameters. Most airflow sensors detect apnoeas reliably, but the detection and quantification of decreased flow needed to diagnose hypopnoeas depends on the type of sensor used. Hypopnoeas make up the majority of obstructive respiratory events[46] and therefore measurement needs to be reliable. Oronasal airflow can be measured using thermistors which detect changes in temperature with respiration. Unfortunately, the response is not linear and therefore they cannot be used to determine hypopnoeas reliably. Furthermore, their accuracy varies greatly depending on the position of the sensors, the sleep position of the patient, the presence of nasal obstruction, and the make of the thermoelement used.[56] For these reasons the ASDA Task Force does not recommend thermoelements for the detection of obstructive respiratory events.[20] Despite this, they continue to be used for flow detection in many commercially available sleep diagnostic systems. Nasal pressure sensors connected to the nose via nasal prongs are more accurate than thermoelements in detecting hypopnoeas.[57] However, nasal pressure is falsely increased in the presence of nasal obstruction and there is a non-linear relation between nasal pressure and nasal flow. Square root linearisation of nasal pressure greatly increases the accuracy for quantifying hypopnoeas and detecting flow limitation.[58 59] Mouth breathing can affect the measurement but pure mouth breathing is uncommon.[60]

Respiratory effort can be assessed in a number of different ways. Chest and abdominal wall motion can be measured by strain gauges, pressure transducers, or by measuring the impedance of wires placed around the chest and abdomen. This allows the distinction between central events, characterised by a reduction in respiratory effort, and obstructive events in which efforts continue, usually with a phase shift between chest wall and abdominal wall motion; as the diaphragm descends the abdomen moves out but, because of upper airway obstruction, the thorax is subjected to large negative pressures and is sucked in. Respiratory inductance plethysmography (RIP) detects changes in the volume of the chest and abdomen during inspiration and expiration and, when properly calibrated, the sum of the two signals can provide an estimate of tidal volume.[61] However, calibration may be difficult to maintain throughout the night.[62] RIP allows an acceptable semi-quantitative measurement of ventilation and therefore hypopnoeas. The ASDA Task Force recommends the use of RIP or measurement of nasal

pressure using nasal cannulae to detect airflow and ventilation.[20]

Monitoring of sleep

Sleep quality and stage is monitored by electroencephalography (EEG), electro-oculography (EOG), chin electromyography (EMG) and analysed by criteria agreed in the 1960s.[63] These have been modified subsequently, in particular with the recognition that much shorter periods of arousal (so called "micro arousals") may be important. Electrophysiological monitoring allows confirmation that sleep has taken place, gives data about the amounts of different sleep stages and sleep quality, and can quantify the number of arousals which might reasonably be expected to be a good predictor of one of the most important symptoms of obstructive sleep apnoea—namely, EDS. Unfortunately, a number of studies have failed to show any relationship between the arousal index or any other of the sleep quality variables with daytime symptoms.[49 64 65] Furthermore, there is poor reproducibility of the scoring of arousals.[66] Douglas *et al*[67] showed that the addition of electrophysiological analysis of sleep did not alter the diagnosis in 200 consecutive patients being investigated for possible OSAHS. It could be diagnosed as accurately by measuring the number of apnoeas + hypopnoeas per time in bed as by the number of apnoeas + hypopnoeas per time asleep (AHI).

Despite its widespread use and many advocates, the evidence does not support the need for full PSG in the routine diagnosis of OSAHS. One other approach to the recording of sleep is wrist activity monitoring. Although it is not recommended routinely in the diagnosis, it may be a useful adjunct to a detailed history in the assessment of sleep disorders.[68]

Objective confirmation of OSAHS

Various different approaches have been developed. These range through attended full PSG, unattended full PSG, limited PSG to oximetry, or movement detectors alone. Split night studies have been used; in patients with an AHI of >40 recorded in the first 2 hours of PSG the diagnosis of OSAHS can be made reliably without proceeding to a full night study. The second part of the night can be used for continuous positive airway pressure (CPAP) titration with accurate CPAP estimation.[45] There is a trend for studies to be performed in the patient's home rather than hospital. Home studies have the theoretical advantage that patients can sleep in their own environment without occupying a hospital sleep laboratory bed, providing more representative data in a cost effective way.[69] Failure due to technical problems can occur in 5–20% of cases.[45 70] Repeat testing increases costs. Factors such as patient disability or transportation problems make home studies impractical for some.[71] Further validation and evaluation of the cost effectiveness of home studies is required.

Limited sleep studies usually quantify obstructive respiratory events without recording sleep. They typically include the measurement of oronasal airflow, chest wall and abdominal effort, ECG and oxygen saturation (Spo_2). In addition, leg and eye movement, body position, and snoring may be recorded. The systems are usually portable and can be used at home. The potential advantages of these systems are that they are cheaper, less labour and time intensive, and technically less challenging. The main disadvantage is that the lack of sleep recording leads to uncertainty when deciding if respiratory events occur during wakefulness or sleep. Surrogates of sleep such as motion detectors[72] and static beds[73] attempt to estimate times of wakefulness but are poorly validated and do not appear to improve sensitivity or specificity.[45] Furthermore, the study by Douglas *et al*[45] suggests that documentation of sleep does not affect the final diagnosis. Generally, there is good correlation between the AHI obtained from limited channel devices and PSG.[74] The sensitivities and specificities of limited in-laboratory devices are 82–94% and 82–100%, respectively.[75 76] A systematic review in 1997 concluded that full PSG may not be necessary to diagnose OSAHS and that limited in-laboratory cardiorespiratory studies in patients with a clinical suspicion of OSAHS may suffice.[77]

Newer techniques

The effects of the large intrapleural pressure swings during obstructive respiratory events on the autonomic nervous system, pulse, and blood pressure have given rise to the development of newer non-invasive techniques to measure apnoea or hypopnoea.

Indirect measurement of peripheral vasoconstriction and transient tachycardia through a finger plethysmograph,[78] analysis of very low frequency components of heart rate variability,[79] and the measurement of the change of pulse transit time[80] during apnoeas have revealed promising results. Furthermore, pulse transit time can be used to differentiate between obstructive and central events.[81]

Pulse oximetry

Transcutaneous nocturnal pulse oximetry is increasingly being used for initial screening for OSAHS as it is inexpensive and can be simply applied and interpreted.[47] Oxygen desaturations are common with obstructive apnoeas but can be absent with hypopnoeas or in events with increased upper airway resistance. They also occur frequently in other cardiovascular and respiratory conditions unrelated to airway obstruction, resulting in false positive results. The parameters reported vary widely but include total number of desaturations, oxygen desaturation index (ODI), desaturations per hour, highest, lowest and mean Spo_2, and cumulative time Spo_2 spent below 90%. A 4% desaturation is most commonly considered to be significant, but 3% and 5% desaturations are also used. As with the AHI criteria, there is no consensus as to the ODI which represents a normal or abnormal result but commonly used thresholds are ODI >5, >10, and >15. Nocturnal artefacts, inaccurate readings in obese patients, and the presence of hypotension and haemoglobin abnormalities can limit the accuracy of the results. Devices with low sampling rates, used in some home pulse oximeters to preserve memory, can significantly underestimate oxygen dips.[82] Furthermore, it is important for there to be a visual print out of the oximeter trace; artefacts are more easily seen and the pattern of oximetry may indicate that the calculated AHI may be an underestimate—for instance, if the patient did not sleep for a period of the night.

The sensitivity of nocturnal pulse oximetry in the diagnosis of OSAHS ranges from 31% to 98% and specificity from 41% to 100%. This wide range of reported sensitivities and specificities results from the great diversity in criteria definition, populations studied, and devices used.[83] In the study by Douglas *et al* 66% of patients with OSAHS could be diagnosed with oximetry alone, but many of the patients undiagnosed by oximetry had moderately severe OSAHS and benefited from treatment.[67] Nocturnal pulse oximetry performed prospectively in 275 patients suspected of OSAHS in the laboratory and compared with full PSG reported sensitivities of 80%, 71% and 63% and specificities of 89%, 93% and 99% for ODIs of >5, >10, and >15, respectively.[84] The authors argued that the number of full PSG recordings could be reduced by up to 50% using nocturnal pulse oximetry.

Pulse oximetry is probably most useful in patients with a high suspicion for OSAHS based on clinical features.[83 85 86] The combination of a high ODI and high pretest clinical suspicion can be regarded as sufficient to make a diagnosis of

OSAHS. Patients with suspected OSAHS who have a negative pulse oximetry trace or have significant concurrent respiratory or cardiovascular disease need further investigation.[47] It may also be useful in excluding sleep apnoea in snorers with a low clinical suspicion for OSAHS.[47] The 4% dip rate has been shown to be the best oximetry derived variable predicting symptomatic benefit from CPAP.[48]

CONCLUSION

The history and examination are key to making the diagnosis of OSAHS and are sometimes overlooked in the debate about which technology is most appropriate. The history should be targeted towards making the diagnosis, but also assessing disease severity, the impact on social and occupational function, as well as on the patient's quality of life. The presence of significant cardiovascular, respiratory, and neurological co-morbidity should also be determined. This assessment should include the bed partner's report whenever possible. In a significant proportion of patients the diagnosis can be made by oximetry alone, and in most of the remainder by limited PSG although close attention needs to be given to the parameters recorded and the instruments used. Full PSG remains useful in research and for occasional patients who cannot be diagnosed using the simpler strategies. The future lies in the development of less intrusive systems to identify accurately those patients most likely to benefit from treatment.

Authors' affiliations
D Schlosshan, M W Elliott, Department of Respiratory Medicine, St James's University Hospital, Leeds LS9 7TF, UK

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Revised

510(k) Number (if known): K011723

Device Name: Anti-Snoring Device

Indications For Use:

The Anti-Snoring Device is intended for use in stiffening the soft palate tissue which may reduce the severity of snoring in some individuals.

Concurrence of CDRH, Office of Device Evaluation (ODE)

Susan Runner

(Division Sign-Off)
Division of Anesthesiology, General Hospital, Infection Control, Dental Devices

510(k) Number: K011723

Indications for Use

510(k) Number (if known): K040417

Device Name: Pillar™ Palatal Implant System

Indications for Use: The Pillar™ Palatal Implant System is intended for the reduction of the incidence of airway obstructions in patients suffering from mild to moderate OSA (Obstructive Sleep Apnea).

Prescription Use _X_ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Susan Runner

(Division Sign-Off)
Division of Anesthesiology, General Hospital, Infection Control, Dental Devices

510(k) Number: K040417

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Radiofrequency Ablation for the Treatment of Mild to Moderate Obstructive Sleep Apnea

Marc Bernard Blumen, MD; Serge Dahan, MD; Bernard Fleury, MD; Chantal Hausser-Hauw, MD; Frederic Chabolle, MD

Objectives/Hypothesis: **Obstructive sleep apnea syndrome is due to pharyngeal obstructions, which can take place at the level of the soft palate. Temperature-controlled radiofrequency ablation has been introduced as being capable of reducing soft tissue volume and excessive compliance. The aim of the study was to evaluate prospectively the possible efficacy of temperature-controlled radiofrequency ablation applied to the soft palate in subjects with mild to moderate obstructive sleep apnea syndrome.** ***Study Design:*** **Twenty-nine patients with a respiratory disturbance index between 10 and 30 events per hour, body mass index equal to or less than 30 [illegible] level of the soft palate were included in a pilot, prospective nonrandomized study.** ***Methods:*** **Snoring and daytime sleepiness were evaluated subjectively. Treatment (maximum of three sessions) was discontinued when the bed partner was satisfied with the snoring level. A full night recording was performed at least 4 months after the last treatment.** ***Results:*** **Mean snoring level decreased significantly from 8.6 ± 1.3 to 3.3 ± 2.5 on a visual analogue scale (0–10). Daytime sleepiness decreased nonsignificantly. Mean respiratory disturbance index decreased significantly from 19.0 ± 6.1 events per hour to 9.8 ± 8.6 events per hour. Mean lowest oxygen saturation value increased nonsignificantly from 85.3% ± 4.1% to 86.4% ± 4.4%. Of the patients, 65.5% were cured of their disease.** ***Conclusions:*** **Temperature-controlled radiofrequency ablation was effective in selected patients with mild to moderate obstructive sleep apnea syndrome. A full-night polysomnography is required after completion of treatment to rule out residual disease.** ***Key Words:*** **Snoring, obstructive sleep apnea syndrome, radiofrequency ablation, soft palate, treatment.**

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From the Department of Otolaryngology—Head and Neck Surgery (M.B.B., S.D., F.C.) and the Sleep Laboratory (B.F., C.H-H.), Foch Hospital, Suresnes, France.

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Send Correspondence to Frederic Chabolle, MD, Department of Otolaryngology—Head and Neck Surgery, Foch Hospital, 40 rue Worth, 92150 Suresnes, France. E-mail: f.chabolle@hopital-foch.org

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is present in 2% to 4% of the general population.[1] It is associated with excessive daytime sleepiness, snoring, and cardiovascular complications. Obstructive events occur at the level of the pharynx. Obstructions can be diffuse or localized either at the retrolingual site or the retropalatal level. They are due to excessive tissue in a normal skeletal "box," normal-sized tissue in a small squelettal "box," or presence of tissue with excessive compliance.

Several surgical treatments have been advocated to treat OSAS. They are either global, treating the diffuse [illegible] with maxillary advancement, or more specific, aiming at the soft palate or base of tongue. Uvulopalatopharyngoplasty since 1981[2] and laser assisted-uvulopalatopharyngoplasty (LAUP) since 1994[3] have been proposed to treat excessive soft tissue at the level of the soft palate. In 1998, Powell et al.[4] described a new technique using temperature-controlled radiofrequency (TCRF) waves to reduce volume and rigidify it (somnoplasty). When TCRF ablation was applied to the soft palate, there were no severe adverse effects and the uvula's length was reduced.[4,5] Several other authors have shown that somnoplasty applied to the soft palate of patients with simple snoring, upper airway resistance syndrome, or mild sleep apnea syndrome (with a respiratory disturbance index [RDI] <15) could reduce snoring, respiratory efforts, and daytime sleepiness.[4,6] These two studies failed to demonstrate a significant reduction in the number of obstructive events.

Patients with OSAS caused by excessive compliance or tissue hypertrophy, or both, may benefit from radiofrequency ablation. The aim of our study was to evaluate a possible efficacy of radiofrequency ablation with thermal control on selected patients with OSAS on a short-term basis.

PATIENTS AND METHODS

We conducted a pilot, prospective, nonrandomized study at Foch Hospital (Suresnes, France) from October 1998 to March 2001. Patients were physician-referred or self-referred to the

medical center's otolaryngology clinic. All patients were seeking treatment for habitual snoring or sleep apnea. Patients answered a standard questionnaire including age, sex, weight, height, medical history and past surgery, habitual smoking, or alcohol consumption. A complete otolaryngological examination was performed, including a fiberoptic pharyngoscopy with and without Müller maneuver. A sleep study was requested for all patients, either a full polysomnography (level I or II) or a cardiorespiratory recording (level III). Patients who had none (probable simple snoring) or all of the following signs of probable severe sleep apnea syndrome (habitual snoring, daytime sleepiness, apnea witnessed by the bed partner, history of cardiovascular disease, and morbid obesity) were assessed by level III recordings. The other patients were assessed with level I or II polysomnography.

Polysomnographic Methods

Level I polysomnography is defined as a full polysomnographic study in the hospital sleep laboratory. Level II polysomnography is defined as a full polysomnographic study that was performed in an ambulatory setting. Both consisted of recordings of electroencephalogram (C3/A2 and O2/A1 electrodes of the international electrode placement system), electro-oculogram, chin electromyogram, and electrocardiogram. Respiration was monitored by nasal and buccal thermistors until 1999, then with a pneumotachograph for some polysomnographic studies. Airflow and thoracoabdominal movements were monitored to distinguish between central and obstructive breathing disorders. Oxygen saturation was recorded by means of pulse oximetry. Level III polysomnography is an ambulatory study measuring nasal and oral airflow, chest wall impedance, oxygen saturation, and heart rate.

An apneic event was defined as cessation of airflow for at least 10 seconds. A hypopneic event was defined as a decrease in airflow of greater than 50% associated with a drop in oxygen saturation greater than 3% and/or a microarousal (when level I or II polysomnography was performed). The study was scored for presence of apnea, hypopnea, and change in oxygen saturation. Sleep–wake stages and arousals were scored in polysomnography level I and II using previously published data.[7]

Indications for treatment of mild to moderate obstructive sleep apnea followed a specific decision tree. All patients were advised on behavior modifications (loss of weight, avoidance of tobacco or alcohol, anxiolytic consumption, or a combination of these), dental appliances, and continuous positive airway pressure. If these measures were refused or had been attempted previously, three surgical treatment options on the soft palate could be offered: TCRF ablation, LAUP, or uvulopalatopharyngoplasty (UPPP). These surgical options were offered only if the patients fulfilled the following elements: an RDI between 10 and 30 events per hour, airway obstruction visualized clinically and during the Müller maneuver primarily at the level of the soft palate, and no morbid obesity, as defined by a body mass index (BMI) greater than 30 kg/m^2.

On a routine basis, recommendations were made by the physician toward one of the three treatment options based on the decision tree. Uvulopalatopharyngoplasty was recommended in case of tonsil hypertrophy or a nasal obstruction linked to a septal deformation (or both). Laser assisted-uvulopalatopharyngoplasty was recommended in case of a long uvula, moderate tonsil hypertrophy, or the presence of nasal obstruction linked to inferior turbinate hypertrophy (or a combination of these). Temperature-controlled radiofrequency ablation was recommended in case of absence of moderate to major tonsil hypertrophy or if nasal obstruction linked to inferior turbinate hypertrophy was present (or both). The final therapeutical option was chosen after reviewing results, possible side effects, and complication rates of each of the treatment options with the patient. Information consent was obtained from each patient.

The inclusion/exclusion criteria of the present study were stringed and were as follows: TCRF procedure on the soft palate alone, no or mild nasal obstruction complaint, no history of surgery on the soft palate, no active upper airway infection or blood coagulation abnormalities, and a follow-up clinical examination and sleep study.

Procedures and Postoperative Temperature-Controlled Radiofrequency Evaluation

All procedures were performed by two physicians. Each patient received local anesthesia; Xylocaine was first sprayed on the tongue and oral cavity. After this, 2 to 10 mL 1% lidocaine with 1:100,000 epinephrine was injected at the sites of treatment. The procedures were performed in a surgical room in an ambulatory mode.

Somnoplasty Procedure

The equipment used included, first, a 215 radiofrequency control unit (Somnus Medical Technologies Inc., Sunnyvale, CA) and, second, a [illegible] control unit (Somnus Medical [illegible] a sterile, single-use handpiece, consisting of [illegible] a total length of 2.0 cm (with 1 cm active and 1 cm insulated). Two thermocouples, one at the tip of the electrode and one at the insulation, continuously monitor temperature and impedance during electrode penetration and treatment. A dispersive electrode was applied to the patient's back to return current to the control unit.

Maximum power was set at 10 W. Maximum target temperature was 85°C. Three protocols using different levels of energy were successively used in time: total energy per session of 1300 J with three lesions (protocol 1, from October 1998 to December 1998), 2800 J with four lesions (protocol 2, from January 1999 to June 1999) and 2100 J with three lesions (protocol 3, from July 1999 to December 2000) (Fig. 1). The last polysomnographic studies were performed in March 2001. Levels of energy were not based on the soft palate aspect (thickness, length of the uvula). They were part of a search for the appropriate level of energy.

Panel A Panel B Panel C

Fig. 1. Three protocols with different total energies per session: (A) 1300 J, (B) 2800 J, and (C) 2100 J.

Energy delivery during the session was stopped if pain or blanching of the mucosa occurred. The precise energy delivered was recorded. No uvulectomies were performed.

A soft diet was recommended for 2 days after treatment. Paracetamol was prescribed in case of discomfort or pain. Steroids (prednisone, 20 mg/tablet) were prescribed at the dosage of 1 mg/kg for 1 day or more if "a swelling sensation in the back of the throat" was noted.

Evaluation

Evaluation of efficacy of somnoplasty was assessed subjectively by the patient and the patient's bed partner and objectively by a polysomnographic study (level I, II, or III).

Subjective evaluation. The bed partner evaluated the snoring volume on a visual analogue scale (VAS) ranging from 0 (no snoring) to 10 (snoring loud enough to be heard from another room or the bed partner has to leave the room to sleep elsewhere).[4] On the VAS, levels of 1 to 3 were considered loud respiration; 4 to 6, moderate snoring; 7 to 8, loud snoring; and 9 or 10, very loud snoring. Satisfaction of the bed partner was also assessed.

The patient evaluated his or her somnolence on the standardized Epworth Sleepiness scale. Absence of daytime sleepiness was defined as a score equal to or less than 8.

Subjective evaluation of snoring and sleepiness using the same scales took place before treatment and was scheduled for 6 to 8 weeks after each treatment session. A clinical examination of the soft palate was performed 6 to 8 weeks after the treatment session, determining the presence of any mucosal/uvula lesions. This examination could occur earlier if the patient felt a severe pain despite analgesic intake for more than 2 days.

Objective evaluation. Respiratory parameters (apnea and hypopnea index, minimum oxygen saturation) were assessed by a level I, II, or III polysomnographic study. Objective evaluation took place at least 4 months after the last treatment session. The last treatment session was defined arbitrarily as the session when 1) the bed partner was satisfied with the snoring volume after TCRF ablation, the snoring not being disturbing anymore, or 2) the bed partner was not satisfied with the snoring volume after TCRF ablation and the patient wished to stop TCRF treatment or change to another treatment (LAUP).

No more than three treatment sessions were performed, with an interval of 6 to 8 weeks between each treatment session. The patients were advised that they would probably need two or three treatment sessions.

The level of postoperative polysomnography (I, II, or III) was chosen regarding the success on snoring and daytime sleepiness. If treatment was effective on snoring but not on somnolence, a level I or II polysomnographic study was prescribed; nevertheless, if level I or II polysomnography was not available at the moment of necessary recording, a level III polysomnographic study was performed.

Criteria for Success and Statistical Analysis

Success on snoring was defined by a final snoring score on VAS of 3 or less and a satisfied bed partner. Improvement was defined as a final snoring volume lower than preoperative.

Cure of sleep apnea was defined as an RDI below 10 events per hour. Temperature-controlled radiofrequency was considered an effective treatment if the RDI after TCRF ablation was less than 20 events per hour with a reduction greater than 50% from the baseline RDI.

All results are expressed as the mean ± SD. Data were analyzed (Statview for Windows, version 5.0, SAS Institute Inc.) using a Student paired *t* test. Linear regression was used to appreciate the relationship between different parameters. A *P* value less than .05 was considered significant.

RESULTS

One hundred fifty-five patients with obstructive sleep apnea fulfilled our criteria of a possible surgical procedure on the soft palate and accepted to go to "surgery." Forty-seven patients elected to undergo UPPP; 30 patients, LAUP; and 78 patients, TCRF. Among the 78 patients, 37 did not come back after the first treatment session or for a second treatment session. Forty-three patients had a full course of treatment (i.e., were evaluated clinically after the last treatment session as we defined it previously). Four of them had a simultaneous treatment at two sites: soft palate and inferior turbinates. They were not included in the study.

Twenty-nine patients (26 males and 3 female patients) completed the study clinically and with post-treatment polysomnography. Mean clinical and polysomnographic follow-up times, respectively, were 11.0 ± 4.7 weeks and 8.5 ± 3.8 months after the last procedure. Mean age and BMI were 57.4 ± 9.2 years and 25.7 ± 2.7 kg/m^2, respectively.

Two patients were treated with protocol 1, 11 with protocol 2, and 16 with protocol 3. Mean number of sessions was, in protocol 1, 2.5 ± 0.7; in protocol 2, 2.0 ± 0.6; and in protocol 3, 2.1 ± 0.7. Mean total energy delivery per session was, in protocol 1, 1387 ± 62 J; in protocol 2, 2719 ± 106 J; and in protocol 3, 2170 ± 100 J. Mean BMI after TCRF ablation was not significantly different from baseline (P = .5). Results are presented pooled in terms of [illegible] of the small number of patients [illegible].

[illegible] improved in 96.6% of the patients (28 of 29). In none of the patients did snoring get worse. Mean snoring level decreased significantly from 8.6 ± 1.3 to 3.3 ± 2.5 (P <.0001), and 86.2% of the bed partners were satisfied. Success of the treatment on snoring based on a VAS score of 3 or less and a satisfied bed partner was 65.5%.

Daytime sleepiness based on Epworth Sleepiness scale score improved in 62.1% of the patients (18 of 29). Mean Epworth Sleepiness scale score decreased nonsignificantly from 7.3 ± 3.6 to 6.3 ± 3.9 (P = .15). Daytime sleepiness with an Epworth Sleepiness scale score greater than 10 was found in 20.7% (6 of 29) of the patients.

The level of polysomnography before or after TCRF ablation did not seem to influence the outcome. The level of polysomnography before or after TCRF ablation for each patient is shown in Figure 2.

Mean apnea and hypopnea indexes before and after TCRF ablation are shown in Figure 3. The RDI values for the 29 patients before and after TCRF ablation are shown in Figure 2. Respiratory disturbance index values improved in 86.2% of the patients (25 of 29); in 13.8% (4 of 29) of the patients RDI values got worse. Mean RDI decreased from 19.0 ± 6.0 events per hour to 9.8 ± 8.6 events per hour (P <.0001). Obstructive sleep apnea syndrome was cured in 65.5% of the patients (19 of 29). Treatment was effective in 65.5% of the patients (19 of 29).

Among the 19 patients who were cured, 4 patients remained sleepy according to their Epworth Sleepiness

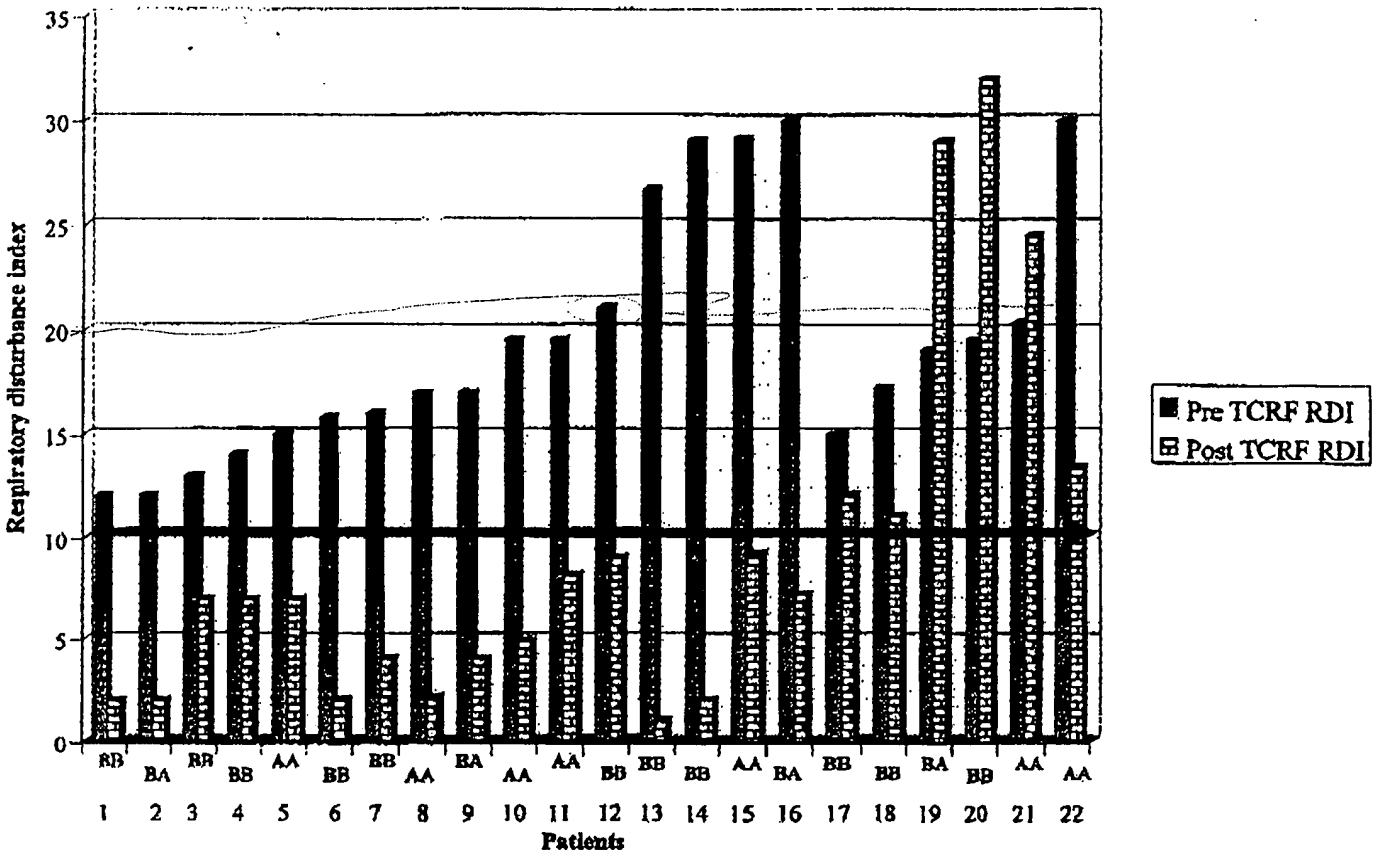

Fig. 2. Respiratory disturbance indexes of total population before and after temperature-controlled radiofrequency ablation. (A) Level I or II polysomnography. (B) Level III polysomnography.

scale scores. These four patients had a high number of microarousals (25 ± 16.7 microarousals per hour of sleep) on the polysomnography after TCRF ablation. In one patient, the abnormal level of microarousals was related to periodic limb movements. In the other three patients, these microarousals might have been related to limitation flow. Mean minimal oxygen saturation increased nonsignificantly from 85.3% ± 4.1% to 86.4 ± 4.4% ($P = .35$). This decrease is associated with a significant decrease of the snoring volume.

No patients complained of any respiratory distress, hemorrhage, or cardiovascular complications in the postoperative period. Three soft palate perforations occurred in protocol 2, with spontaneous healing in two cases. The third patient had a persistent hole of 5 mm in diameter, which gave a whistling sound to his respiration during sleep. No uvula necrosis was observed.

Body mass index, age, length of the uvula, thickness of the soft palate on clinical examination, dental class, Epworth Sleepiness scale score, snoring volume, and severity of OSAS by the RDI did not correlate with the outcome.

DISCUSSION

The main goal of the present study was to evaluate a possible efficacy of radiofrequency ablation with thermal control applied on the soft palate of selected patients with mild to moderate sleep apnea. The main finding of the present study is that in selected patients, TCRF ablation can significantly reduce the RDI in subjects with OSAS.

The definitions of cure and success rate were taken from the international literature. In most of the sleep institutions, OSAS is defined by an RDI greater than 10 events per hour. Therefore, cure of OSAS occurs when the patient's RDI is less than 10. Most of the reports have defined "success" as a reduction of preoperative RDI of more than 50% and a postoperative RDI less than 20.[9] The term "success" being closer to the term "cure," we chose to define this state as the treatment efficacy.

Uvulopalatopharyngoplasty is the only soft palate surgical technique recommended by the American Sleep Disorders Association because of its demonstrated efficacy on OSAS.[10] In particular, the efficacy rate of UPPP was evaluated in the meta-analysis of Sher et al.[9] It was estimated to be 40.7%. Studies included in the meta-analysis of Sher et al.[9] often aimed at efficacy and did not always take into account all the specific outcome predictive factors. Indeed, in the meta-analysis of Sher et al.,[9] as well as in other publications, several factors were shown to give poorer results, especially in subjects with higher BMI,[11] nontreated sites of obstruction and severe OSAS.[11–15]

Although Sher et al.[9] and other authors[12,13] did not find any significant difference in BMI between UPPP success and failure, some authors, such as Chabolle et al.,[11] showed that a BMI exceeding 27 kg/m^2 gave poorer results. Indeed, obesity can be responsible for UPPP failures

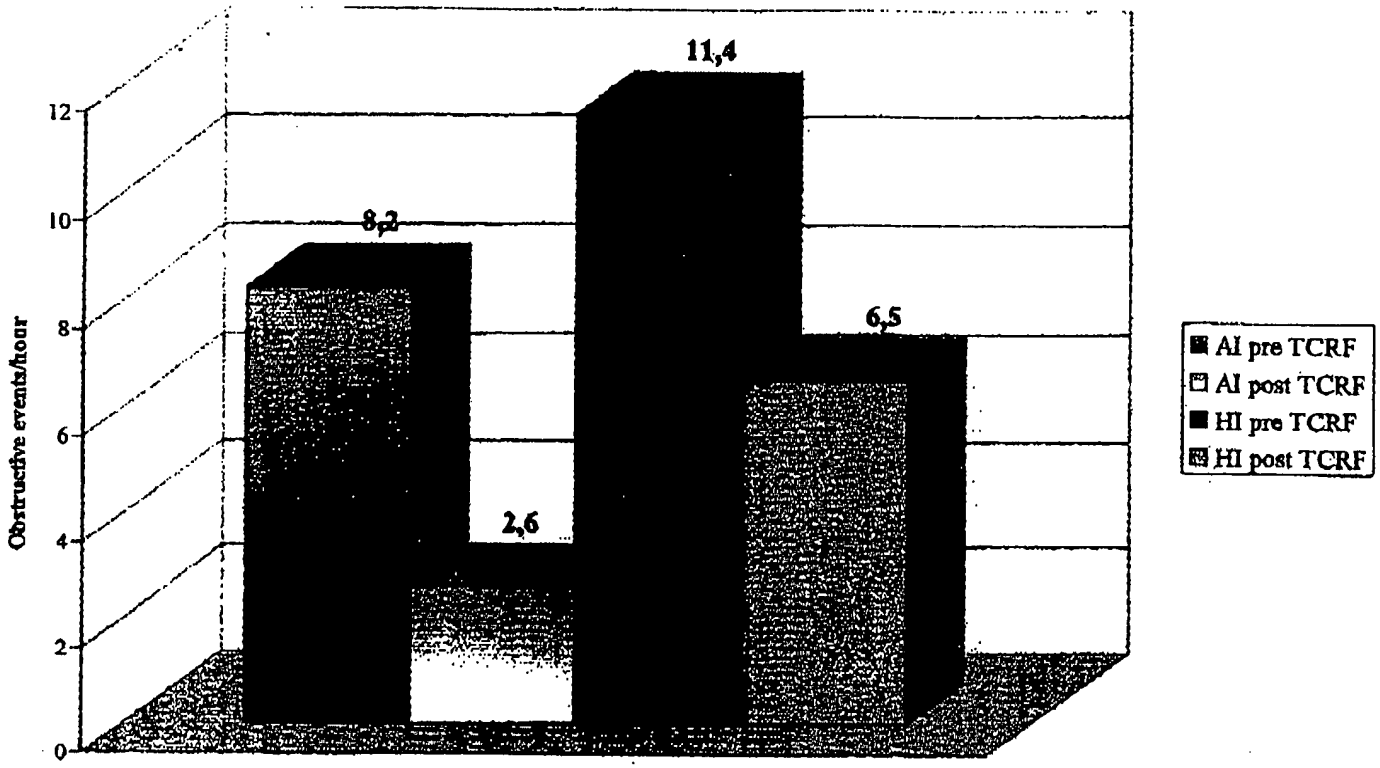

Fig. 3. Apnea and hypopnea indexes before and after temperature-controlled radiofrequency ablation. AI = apnea index; HI = hypopnea index.

because of factors that are not addressed by surgery: compromised respiration (over[illegible] compliance.[17] Fat can also infiltrate pharyngeal tissue. When fat is located around the pharynx,[18] it is [illegible] ble by UPPP.

Site of obstruction can be assessed by several means, such as fiberoptic awake endoscopy with or without Müller maneuver, airway manometry, asleep endoscopy with or without continuous positive airway pressure, or imaging. Although some techniques greatly improve UPPP outcome, they are difficult to use in standard clinical practice.[14] There is no universally validated method to determine precisely the site of obstruction. The methods recommended by Sher et al.[9] are fiberoptic endoscopy and lateral cephalometry. Lateral radiographic cephalometrics, although performed with the patient awake and seated upright, and best for bony structures and not for airway spaces or tissue volume, may give information regarding the site of obstruction. A retrolingual site of obstruction may be pointed out by a low position of the hyoid bone and by a narrowed posterior airway space secondary to a large tongue or retrognathia. A retrovelar site of obstruction could be pointed out by an increased uvula length. Millman et al.[12] showed that a lower position of the hyoid bone and presence of retrognathia could greatly decrease the likelihood of a positive outcome. Woodson and Conley[16] showed that in retrognathic patients, the presence of a small posterior airway space and position of the hyoid bone were negative outcome predictive factors. Doghramji et al.[19] showed that success tended to be greater when uvula length was longer.

It seems obvious that determination of the site of obstruction is crucial when deciding a site-specific surgical procedure. [illegible] showed that patients with a retrovelar site of obstruction (type I obstruction) had a 52.9% success rate compared with 5.3% for patients with a combined site of obstruction (tongue and soft palate [type II obstruction]) or a tongue base obstruction (type III obstruction). Site of obstruction also seems to be linked to the number of obstructive events. Sher et al.[9] showed that the RDI and, even more, the apnea index, were greater when comparing patients with type I obstruction versus those with types II and III obstruction.

Severity of OSAS probably should be taken into account, especially since Sher et al.[9] showed that responders (RDI of less than 20 and a 50% decrease from preoperative RDI) had a lower baseline (43.1 ± 26.3 vs. 65.7 ± 26.7). Chabolle et al.[11] found a cut-off point at 30 events per hour of sleep. Cure rate was 80% when the RDI was less than 20 as opposed to 27% when it was greater than 30 events per hour.

The patients in the present study were selected according to stringent criteria: soft palate as the site of obstruction, a BMI less than 30 kg/m^2, and an RDI of less than 30 events per hour. The treatment failures in the present study may have had an associated tongue base obstruction during the night, although it was not observed during clinical examination, even with Müller maneuver. A cephalometric analysis may have been useful to determine whether the subject had a possible tongue base obstruction.

The treatment failures may have also been due to residual excessive tissue in the soft palate. Radiofrequency ablation has been shown to reduce tongue tissue in animals.[20] On the human soft palate, using a mean total energy level of 2377 J in one to several sites, a reduction of volume was shown by Powell et al.[4] Shrinkage in uvula length, but not in width, was observed. This shrinkage may be attributed to the scarring process, which is thought to rigidify the soft palate and decreases excessive compliance. Reduction of volume by necrosis may only be obtained using higher levels of energies. This may not be possible because of potential side effects such as postoperative edema, which may compromise the airway, and mucosa necrosis, which may lead to perforation or uvula destruction. Therefore, using lower energies may provide only a nonsignificant volume reduction by necrosis, a probable volume reduction by retraction, and a decrease in compliance. Although not significant in our study, a long uvula should probably not, for the reasons mentioned earlier, be the best indication for radiofrequency ablation in OSAS.

The time to stop treating a patient is another possible factor that might have lowered one or the other, success rate and/or cure rate. Our protocol stated that treatment should be stopped when the subject's bed partner was satisfied with the snoring level. This evaluation is highly subjective. Post-treatment snoring levels on the VAS were greater for patients who were considered failures with TCRF ablation. This may mean that treatment was insufficient and the patient may require more sessions. Because of the high cost of the electrodes and a probable treatment of all the soft palate [illegible] ablation, we limited the number of sessions to [illegible] proposed another [illegible] option.

Snoring is not the best method to determine when to stop treatment because some bed partners were satisfied with the snoring level even though the patients were not cured of their disease; on another hand, some patients, who did not have any significant residual apnea or hypopnea, continued to snore and remained somnolent. Ambulatory oxygen saturation, because of it lower cost and its ease of use, could be one possible tool for evaluation of when to stop the treatment.

A polysomnographic study should be performed in all treated patients. It detects TCRF ablation failures or worsening after treatment. Four patients in our study got worse. Several hypotheses can be made, including occurrence of incidental factors such as sleep deprivation or acute nasal obstruction during the night of the recording or the presence of a new site of obstruction at the level of the tongue base. Critical closing pressure may have been higher in the first place at the level of the soft palate than at the level of the tongue base. After TCRF treatment and a possible lowering of the critical closing pressure at the level of the soft palate, the tongue base may have become the primary site of obstruction.[21,22]

Patients were not highly somnolent at baseline because their mean Epworth sleepiness scale score before TCRF ablation was what is considered normal (7.3 ± 3.5). Six of 29 patients (20.7%) patients had an Epworth sleepiness scale score greater than 10 after TCRF ablation. Among them, four patients, who all had an initial RDI greater than 13 events per hour of sleep, were cured of their OSAS based on polysomnography results following our criteria. One cases was clearly related to periodic limb movements. Three of four patients showed an abnormal number of microarousals, which might have been related to respiratory limitation flow. One hypothesis is that TCRF ablation may have transformed OSAS in upper airway resistance syndrome by changing the soft palate's compliance. The compliance was such that the soft palate no longer collapsed against the posterior pharyngeal wall but increased pharyngeal pressures remained. This hypothesis must be confirmed by a study of OSAS patients with a full-night polysomnographic recording with esophageal pressure measurement before and after TCRF treatment.

CONCLUSION

The soft palate is involved in the constitution of a pharyngeal obstruction in obstructive sleep apnea. In some cases, it could be the only site or the predominant site of obstruction. If patients are not overweight and do not have severe OSAS, palate surgery can have a fairly high success rate. We have shown that radiofrequency ablation with thermal control could, in a small, clinically selected population, have a 65.5% cure rate. Clinical teams should extend the present study to a greater number of patients and on a long-term basis to possibly place radiofrequency ablation as one of the treatment of choice for some patients with mild to moderate obstructive sleep apnea, with the advantage of it being associated with few [illegible]

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